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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/920,272 08/22/97 MILLER

F 08338/024003

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EXAMINER

MURPHY, J

ART UNIT

PAPER NUMBER

1646

18

DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/920,272	Applicant(s) MILLER ET AL.	
	Examiner Joseph F Murphy	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) ☒ Responsive to communication(s) filed on 15 September 1999.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31-48 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31-48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of the CERTIFIED copies of the priority documents have been:
1. ☐ received.
2. ☐ received in Application No. (Series Code / Serial Number) _____.
3. ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- | | |
|---|--|
| 14) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 17) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 15) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 18) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 16) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 19) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Continued Prosecution Application

1. The request filed on 9/15/1999 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/920272 is acceptable and a CPA has been established. An action on the CPA follows.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 46 and 47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 46 and 47 recite the term "pharmaceutical composition" comprising either the isolated precursor cell, or the mitotic progeny of said cells. There is no guidance provided in the specification as to how one of ordinary skill in the art would make and use the claimed invention. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the

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claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Applicant provides guidance in Example 16 (page 28, line 26 to page 32 line 2) in the transplantation of the isolated precursor cells into the caudate-putamen complex of rat brain, whereupon the isolated precursor cells survived. However, Applicant does not disclose the efficacy of such treatments in the relieving the pathophysiology of any disease state. The fact that the isolated precursor cells survived, and even were mitogenically active, does not teach the skilled artisan the manner in which to treat a neurodegenerative disorder by transplantation of isolated olfactory precursor cells. Therefore, it would require undue experimentation for the skilled artisan to make and use the claimed invention.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 31-32, 34-36, 39-40 and 43-45 are rejected under 35 U.S.C. 102(a) as being anticipated by Sosnowski et al. (1995).

Sosnowski et al.(page 38, column 1, second paragraph to column 2, first paragraph) teaches the establishment in primary culture of olfactory epithelium isolated from adult mouse. Based upon immunoreactivity (page 45, column 1, fourth paragraph) to antibodies specific for intermediate filament proteins, the cells present in cultures were identified as neurons, glia or

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epithelial cells. Thus, the disclosure of Sosnowski meets the limitations of claims 31, 32 and 34 through the isolation of progenitor cells from peripheral tissue, in this instance olfactory epithelium, of an adult mammal. The further limitations of claims 35 and 36 are met due to the differentiation of the primary culture cells into neuronal cells, indicating the presence in the isolated olfactory epithelium of neuronal stem and progenitor cells. The astrocytes and oligodendrocytes recited in claims 39 and 45 are both glial cells, which are shown to be present in cultures by immunofluorescence. The cells isolated by Sosnowski et al. have been shown to be multipotent, due to the presence in culture of several cell types, thus meeting the limitation of claim 40. The peripheral tissue utilized by Sosnowski et al. for the establishment of their cultures comprises a sensory receptor, thus meeting the limitations of claims 43 and 44.

4. Claims 31-32, 35-36, 39-40 and 43-45 rejected under 35 U.S.C. 102(b) as being anticipated by Schubert et al. (1985).

Schubert et al. (page 7782, column 1, second paragraph to page 7783, column 1, second paragraph) teach the establishment of primary cultures of olfactory epithelia isolated from juvenile rats. Immunoreactivity to nervous-system specific antibodies indicated the presence of neurons and glia, including astrocytes (page 7783, column 2, fourth paragraph). Thus the disclosure of Schubert et al. meets the limitations of claims 31 and 32 through the isolation of precursor cells from isolated olfactory epithelium. Olfactory epithelium comprises a sensory receptor, thus meeting the limitations of claims 43 and 44. The development in culture of neuronal cells indicates the presence of neural stem cells and neural progenitor cells, thus meeting the limitations of claims 35 and 36. The presence in culture of glial cells, together with

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the presence of neurons meets the limitations of claims 39 and 45, as well as the further limitation of claim 40 for a multipotent cell (see page 7785, column 2, second paragraph).

5. Claims 31-32, 35-36, 39-40, 43-45 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Ronnette et al. (U.S. Patent No. 5,318,907).

Ronnette et al. (column 6 line 58 to column 7 line 46) discloses the isolation of cells from the olfactory epithelium of neonatal rats, and their establishment in primary culture. The presence of both neurons and glial cells is demonstrated through immunoreactivity with antibodies specific for neurons (anti-neuron-specific enolase) and glial cells (anti-glial fibrillary acidic protein) (column 8, lines 34-47). The disclosure of Ronnette et al. meets the limitations of claims 31 and 32 through the isolation of precursor cells from isolated olfactory epithelium. Olfactory epithelium comprises a sensory receptor, thus meeting the limitations of claims 43 and 44. The development in culture of neuronal cells indicates the presence of neural stem cells and neural progenitor cells, thus meeting the limitations of claims 35 and 36. The presence in culture of glial cells, together with the presence of neurons meets the limitations of claims 39 and 45, as well as the further limitation of claim 40 for a multipotent cell. Ronnette et al. discloses a kit, comprising an isolated neuron, thus meeting the limitation of claim 48 for a kit comprising a mitotic or differentiated cell that is the progeny of a precursor cell derived from peripheral tissue comprising a sensory receptor.

6. Claims 31, 37 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Schubert et al. (1985), in light of Fraichard et al. (1995).

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The disclosure of Schubert et al. has been set forth above (see section 4, above). The Examiner has cited Fraichard et al. to show that it is an inherent property of neuroepithelial stem cells to express nestin (page 3183, column 2, second paragraph). Fraichard et al. (page 3185, column 1, second paragraph) discloses it is an inherent property of neurons to express enzymes involved in neurotransmitter metabolism, such as glutamic acid-decarboxylase. The disclosure of Schubert et al. therefore meets the limitations of claims 37 and 38. See MPEP § 2131.01.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 31, 41 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schubert et al (1985) in view of La Salle et al. (1993).

The disclosure of Schubert et al. has been set forth above (see paragraph 4, above). However, Schubert et al. does not disclose isolated precursor cells from olfactory epithelium transfected with a heterologous gene. The disclosure of La Salle (page 259, Figure 1) teaches the use of the adenovirus vector for the delivery of the beta-galactosidase gene. It would have been obvious to one skilled in the art at the time the invention was made to use the adenoviral vector for the transfection of the precursor cells isolated from olfactory epithelium with heterologous genes, including trophic factors. The motivation is provided in the disclosure of La Salle (page 988, column 1, first paragraph), which teaches that the ability to deliver foreign genes and

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promoter elements directly to the nervous system would be desirable for the study of the function and regulation of cloned genes, as well as for gene therapy. Furthermore, La Salle (page 990, column 1, second paragraph) also teaches that in the context of degenerative diseases, it may be possible to express growth factors locally as an alternative to the grafting of fetal cells.

8. Claims 31 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayo et al. (1992) in view of Kaufman et al. (1988).

Mayo et al. discloses isolated precursor cells from mouse tongue (page 257, column 2, third paragraph). Mayo does not disclose the use of postnatal animals as a source for the tongue explants. The disclosure of Kaufman et al. (page 9606, column 2, third paragraph) discloses the isolation of myoblasts from newborn rats. Myoblasts are precursors to mature muscle. Therefore, at the time the invention was made it would have been obvious to a person of ordinary skill in the art to isolate precursor cells from the tongue of postnatal mammals. The motivation for doing so is disclosed in Kaufman et al. (page 9610, column 1, third paragraph) to study the control of replication and activation of promoters of tissue specific transcription and posttranscriptional mechanisms.

Conclusion

9. No claims are allowed.


Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 8:30-5:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell can be reached on 703-308-4310. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4227 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-4310.



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
December 2, 1999


PREMA MERTZ
PRIMARY EXAMINER